nite knowledge of physiology. This boy, like the savage, is left in the field of curiosity and feeling subject to the vicious tendencies of the mob. The mob tendency indicates a morbid field. There is little or no resistance."

Personal letter from LORAN S. WALKER of Los Angeles, California.

TREATMENT OF GENERAL PARALYSIS OF THE INSANE.*

By C. W. MACK, M. D., Assistant Physician, Agnews State Hospital, Agnews, Calif.

Psychiatrists have long looked upon general paralysis of the insane as incurable. When supplied with such facts as the duration and character of the onset in a given case, they could almost predict the time of fatal termination. In the hospitals for the insane these patients rapidly pass from the receiving service to the infirm wards where they go through the stage of slow dissolution as paralysis ensues and the mind loses all but a faint trace of former activity. To see a person in the prime of life suddenly stricken with this disease should call forth our best endeavors to arrest its progress. The utter helplessness of these cases and the limited means at our disposal almost checks our enthusiasm, but, thanks to diligent workers, the outlook for the future is more encouraging.

Paresis furnishes a large percentage of the admissions to hospitals for the insane. The writer has not had access to complete statistics, but has referred to the biennial reports of Michigan institutions on account of having some familiarity with the work done in that state. During the two years ending June 30th, 1912, there were 2580 admissions to the four Michigan asylums, and of these 8.8% were cases of paresis. These figures are fairly correct because most of the diagnoses are made upon laboratory findings. Dr. Christian, in the report of the Pontiac State Hospital, gives a somewhat higher percentage for the institution, and states that the percentage of cases of paresis admitted has more than doubled in the last ten years. Also in the same institution this disease is responsible for the greatest number of deaths. Further investigation is necessary before concluding that the disease is becoming more prevalent. The figures given, however, convince one that it is of considerable importance, and a search should be made for some efficient method of treatment.

The pathology is quite well known to the members of the society, but a few brief statements may not be amiss in order to appreciate more fully the therapeutical principles. The disease involves the spinal cord, brain substance and the meninges. It is a diffuse, destructive process resulting in a grave alteration of the cellular structure of the brain. The pia shows a chronic inflammatory reaction with adhesions to the cortex; the neurones undergo degenerative changes, eventually being destroyed and replaced by proliferation of the neuroglia; the blood vessel walls are thickened and the parilymph spaces packed with lymph cells and plasma cells. The greatest alteration of the cortical cells is in the neighborhood of the blood vessels.

The lesions in the central nervous system have been ascribed to the toxins of early syphilis and not considered an active syphilitic process. Recently, Noguchi and others have found the spirocheta pallida in the cortex of dementia paralytica, both post-mortem and by brain puncture. It is quite possible that these organisms are able to invade the brain because of the injury produced by the long standing infection, but even so, the presence of the spirochetes in the cortex is responsible for the inflammatory reaction producing the clinical picture of paresis. The spirochetes are found deep in the cortical substance away from the blood vessels, making it difficult to reach them through the blood stream, on account of the cellular infiltration of the blood vessel walls. If there was some way to increase the permeability of this bearer so that bactericidal substances could come in contact with the spirochetes, the solution of the problem would be easier.

The constitutional treatment deserves mention before describing specific therapy. The pathology of the disease makes evident the fact that it is a grave toxemia if not a direct infectious disease. Not only the brain but the other viscera show the effects of the toxic process. Patients afflicted with such a condition require special treatment with attention directed to raise the bodily resistance just as much as cases of typhoid fever. The toxemia is indicated by the muscular weakness and nervous symptoms which in the early stages often lead to the diagnosis of neurasthenia. There is need for the restful life, careful nursing and daily medical attention to conserve the recuperative powers, and this can only be insured by institutional care. The startling mental features in these cases usually force upon the friends the necessity of commitment, but unfortunately oftentimes not until the disease is well advanced. The damage to the brain has occurred before the physician has an opportunity to prevent it in the early stages. Is it not possible that institutional physicians too hastily relegate these cases to the background of incurables where they receive only routine treatment? A paralytic, apparently undergoing rapid decline, will sometimes improve, gain in strength and show a return of normal mental life lasting a number of months. Such remissions are not uncommon and surely indicate that under some conditions the reparative processes of the body are capable of arresting, temporarily at least, the destructive lesions. The proper use of resources at our command can aid nature in bringing about a greater degree of resistance if careful attention is paid to the constitutional treatment of these patients.

The advent of the Wassermann reaction has demonstrated the relationship between syphilis and paresis and the finding of the spirocheta pallida in the brain gives an indication for specific therapy. Thus far mercury and potassium iodid have had no influence upon the disease, and permanent results have not been obtained with salvarsan given intravenously. This failure can probably be ex-

* Read before the Santa Clara County Medical Society, February 4, 1914.

plained in the light of the pathology of the disease. The blood vessel walls do not permit the passage of medicinal agents or antibodies into the cortex. It has been shown also that substances introduced into the blood stream do not reach the cerebrospinal fluid. This has led to the use of the cerebrospinal fluid as a medium to convey the curative agent to the seat of the disease; or in other words, subdural injections.

Swift and Ellis, in 1912, introduced the intraspinous injection of salvarsanized serum in the treatment of tabes and its use has been extended to paresis and syphilitic brain disease. The method in brief is as follows: One hour after the intravenous injection of salvarsan, blood is withdrawn from which 12 cc. of serum is collected. This is diluted to 30 cc. with normal salt solution, heated for one-half hour at 56° C., and then injected subdurally between the third and fourth lumbar vertebra. The serum is injected by gravity after the withdrawal of an equal amount of cerebrospinal fluid. These injections are repeated at intervals of two weeks. This procedure has brought forth favorable reports from several sources. As yet, however, enough time has not elapsed to determine its true value, but the results obtained are very promising.

It will be interesting to know the mode of action of the salvarsanized serum when injected subdurally. There are several factors to be considered. The salvarsan itself and the serum with its antibodies, complement and protein splitting ferments. All of these come in contact with the pia, if not absorbed into the cortical substance. Heating at 56° C. probably inactivates the ferments and complement. As for the germicidal action of the salvarsan, it can be said that the original dose given intravenously is very much diluted. The 12 cc. of serum represents but a small part of the total quantity, and this is again diluted when injected into the cerebrospinal fluid. Even with this high dilution, it may be able to destroy the spirochetes. Ehrlich's original assertion was that salvarsan had a chemical affinity for the spirochetes, causing their destruction. The effect of the salvarsanized serum may be due to substances formed in the blood serum and not to the salvarsan itself. The salvarsan in the blood could inactivate the organisms in some other part of the body so that protective ferments would be formed for their parenteral digestion. These immune bodies would then be found in the blood stream, and their injection into the cerebrospinal fluid would be the same as producing the passive immunity by antitoxin. Blood serum without salvarsan is not efficacious. This is proven by a comparison of series of cases under treatment with two cases treated with heated and unheated serum alone. The two controls showed no change aside from what might be expected during the ordinary course of events.

The administration of salvarsanized serum was begun at the Agnews State Hospital four months ago. Twelve cases are now under treatment, making a total of thirty-five injections. The first few cases received 40% serum, while a 50% serum has been used with the later ones—going on the supposition that if a little medicine is good more is better. This increased dosage has produced no ill effects and in one case brought about a prompt drop in the cell count; in fact, the lowest in the series. Some of the early cases have shown enough improvement to deserve comment. One has been discharged very much improved and another sufficiently improved to be paroled, and a third case is much better mentally.

Although all of the cases have not shown a better mental condition since the treatment, there have been changes in the cerebrospinal fluid which are very encouraging. The cell count and the albumen content are a good index of the inflammatory process and give us a means to check up the results. In every instance there has been a pronounced drop in the cell count and in three cases it has returned to normal. At the same time there has been a decrease in the amount of albumen in the fluid. The Wassermann reactions have been made normal in only two cases, but this reaction may be influenced by further treatment.

It cannot be expected that any method of treatment will restore a brain whose cellular elements have been damaged and lost any more than the cavities in a tubercular lung can be replaced with normal lung tissue. If the disease process could be arrested there would still remain some mental defect. The treatment of these cases in the early stages is necessary to obtain the best results. No progress can be made until the disease is studied in the early stages, and this must be left largely to the general practitioner, as these cases are usually not referred to hospitals for the insane until every other means has been exhausted. Now that laboratory methods of diagnosis have been perfected it is comparatively easy to recognize paresis. The differential diagnosis between paresis and cerebrospinal syphilis is difficult and cannot be made upon the laboratory findings alone, but the indications for treatment would be much the same in each case.

The writer does not believe that a too radical statement is made when it is said that every patient with mental trouble should have a cerebrospinal fluid examination. The Wassermann blood examination is not sufficient as a somatic syphilis may be present with any form of mental trouble without syphilitic involvement of the nervous tissues. The cerebrospinal fluid very early gives an indication of the invasion of the central nervous system by the syphilitic process and may be discovered before the advent of mental or neurological symptoms.

The value of lumbar puncture is strikingly revealed by a case now under observation. A boy, twenty-one years of age, with a history of a chancre two years ago, and a mental disturbance extending over four years, came to the hospital in a state of maniacal elation. There was a flight of ideas, distractibility of attention and motor restlessness. These, with a history of recurrent attacks, would lead one to believe that we were dealing with manic depressive insanity, and that

syphilis was only incidental. A lumbar puncture disclosed a high cell count and a positive Wassermann reaction in the fluid. It may be an organic brain disease added to a functional psycosis, but without the fluid examination, the luetic involvement of the central nervous system would have passed unnoticed.

Some mention should be made of prophylaxis. The surest way to prevent general paralysis of the insane is to cure syphilis during the primary or secondary stage. With the refinements in laboratory diagnoses an involvement of the central nervous system during the secondary state of syphilis can be detected in a certain percentage of cases. When this occurs the organisms may only damage the nervous tissues without setting up an active syphilitic brain disease, but the tissues have become predisposed to the infection and it may light up again after a number of years in the form of paresis. If every case of syphilis could be treated thoroughly and followed up with cerebrospinal fluid examinations, this complication might be prevented. Those cases showing positive fluids could be given more intensive treatment. If salvarsanized serum is proven to be beneficial in combating syphilis of the central nervous system, this method could be resorted to whenever the fluid shows a positive reaction. Such cases could also report for lumbar puncture, and be given special directions in regard to the life they should lead to prevent the inception of syphilitic brain disease. There is reason to believe that alcohol is particularly injurious, and, not only makes the treatment of syphilis difficult, but renders the individual more liable to the cerebral manifestations of the disease.

The writer has attempted to give a résumé of the present status of the treatment of general paralysis of the insane without any claim, however, for completeness. Inasmuch as the disease is really a late manifestation of luetic infection, the future history of primary and secondary syphilis treated with salvarsan will be awaited with interest. If it does not bring about the desired result, let us hope that further studies of the pathology, immunity reactions and activities of blood ferments will reveal some way to meet these complications when they arise. The employment of salvarsanized serum may not satisfy all requirements, but, at least, it opens the way for further investigation.

ON THE SWIFT-ELLIS TREATMENT OF CEREBRO-SPINAL SYPHILIS.*

By PHILIP KING BROWN, M. D., and W. T. CUMMINS, M. D., San Francisco.

Neither mercury and iodide nor salvarsan intravenously have succeeded in bringing dependably satisfactory results in the treatment of certain syphilitic lesions of the central nervous system and especially not in the parasyphilitic states of tabes and paresis. The growing knowledge of how small an amount of any curative agent as administered ordinarily is excreted into the cerebrospinal fluid,[15] and the brilliant results from the use of anti-meningitis serum applied locally, make it reasonable that a furtherance of the intra-spinal method may produce satisfactory results in cases of syphilis of the central nervous system resisting ordinary treatment. The spirocheticidal action of salvarsan and the blood serum of recently salvarsanized patients has been demonstrated.

Meirowsky and Hartmann [1] showed that such blood serum had definite therapeutic value when used subcutaneously in patients with lues. Swift and Ellis show [2 3] spirocheticidal action of such serum on the spirochetes of relapsing fever, and they also call attention to the highly irritating effect of even small doses (0.1 of a milligram of salvarsan or neosalvarsan) injected into the spinal canals of monkeys. Wechselmann [4] produced convulsions, paralysis and death in two to four days in rabbits and dogs injected intraspinously with 1 mg. of salvarsan.

Plant [5] refers to the spirocheticidal action of the milk of women treated with 606, but regards the benefit to the children to be due rather to the transfer of immune bodies and warns against hoping for cure except by use of the remedy directly. He also reports favorable improvement of cases of tabes, syphilitic paralysis, etc., from subcutaneous injection of salvarsanized serum.

Gibbs and Calthrop [6] report the favorable result of five or six subcutaneous injections given five days apart, of ten to twenty c. c. of serum from a cantharides blister of patients treated four days before with salvarsan 0.4 gm. intravenously. The lessened Wassermann and general improvement were equal to their experience in cases treated directly.

Gondor [7] reports spirocheticidal action of salvarsanized rats' blood on spirochetes of relapsing fever.

Castelli [8] shows similar action of dilute neosalvarsan on various spirochete.

This establishes definitely the fact that the salvarsanized serum is certainly efficient and suggests the danger of even minute doses of the drug itself injected intraspinously. Reports, however, of the danger of this latter method are still conflicting, but a general deduction may be made from Swift and Ellis' report of experiments on monkeys, as well as authentic reports of trials on human beings, that the method of direct injection of the drug is very dangerous. Wolfsohn in a personal communication reported .007 gm., or about 1:100 of an ordinary dose of 606, administered intraspinously at the Johns Hopkins Hospital with death of the patient after two days of great agony. The cord was edematous and the meninges deeply injected. Swift and Ellis [9] report a case of tabes injected with minute doses of 914 with temporary retention of urine and severe lightning pains. Wechselmann reports [10] injecting neosalvarsan intraspinously in two paretic adults and two congenitally luetic children with no bad results. One of the paretics got .003 neosalvarsan at the first injection and .001 at the second injection two weeks later. The other paretic got .005 of neosalvarsan also with no bad effect. The children got from .001 to .0015 and they, too, suffered no reaction.

Marinesco [11] on the other hand reports using

* Read before the Fresno County Medical Society.